

**Remarks**

Claims 27-32 are added. Support for claims 27-29 is found at Tables 2 and 3, and at page 7, lines 19-24 of the specification. Support for claims 30-32 is found at page 12, lines 26-28 of the specification.

The present invention offers surprising effects achieved through the combination of lactose and mannitol in a solution for the introduction and washout of vitrifiable concentrations of cryoprotectants in a cell, tissue, or organ. Previous to the present invention, the use of mannitol was avoided, since it had been reported to produce paradoxical vascular damage to the kidney (by the very author cited against the present case, Khirabadi, *Cryobiology* 35:358 (1997)). And lactose was known to have inadequate solubility to be used in concentrates, and its solubility in the presence of full-strength vitrification solutions was questionable.

The present inventors discovered unexpectedly that by combining lactose and mannitol in the solution, the limited solubilities of both are overcome and that both remain in solution in the presence of cryoprotectants during cooling and warming to deep subzero temperatures (specification, p. 7, lines 19-30). The combination of lactose and mannitol resulted in this unexpected effect.

The Examiner has rejected claims 1-3, 7, 10-12, 14-16, 19, and 22-23 under 35 U.S.C. 103(a) as allegedly being unpatentable over Khirabadi et al. (U.S. Patent 6,194,137). This rejection is respectfully traversed.

Khirabadi et al. does not disclose the use of lactose and mannitol in the same solution for the introduction and washout of vitrifiable concentrations of cryoprotectants. The

cryoprotectants disclosed by Khirabadi include dimethyl sulfoxide, formamide, 1,2-propanediol, 2,3-butanediol, glycerol, ethylene glycol, n-dimethyl formamide, and 1,3-propanediol (Col. 6, lines 22-26). Further solutions are described in column 6. Since Khirabadi does not disclose or suggest the use of lactose or mannitol in the same solution, Khirabadi does not render the present claims obvious.

The Examiner refers to Col. 9 of Khirabadi, which lists a large number of alleged low molecular weight osmotic buffering agents. This disclosure provides no guidance on which of the many possible combinations to use and represents, at best, an invitation to experiment with all possible combinations of impermeant chemicals from Column 6 and osmotic buffering agents. And Khirabadi completely fails to disclose the unexpected benefits of combining lactose and mannitol in a single solution. Accordingly, the present claims are not made obvious by Khirabadi.

U.S. Patent No. 6,395,467 to Fahy does not cure the deficiencies described above since it too fails to disclose or suggest the use of mannitol and lactose in a solution for the introduction and washout of vitrifiable concentrations of cryoprotectants in a cell, tissue, or organ. Thus, the present invention is not rendered obvious by the combination of Khirabadi in view of Fahy.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

**Conclusion**

In view of the foregoing amendments and remarks, Applicant respectfully submits that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the telephone number listed below so that they may be resolved without the need for additional action and response thereto.

Respectfully submitted,

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